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Tension-type Headache With Medication Overuse: Pathophysiology and Clinical Implications

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Abstract

Tension-type headache (TTH) is the most prevalent primary headache disorder. An important factor in the long-term prognosis of TTH is the overuse of acute medications used to treat headache. There are many reasons why patients with TTH overuse acute medications, including biobehavioral influences, dependency, and a lack of patient education. Chronic daily headache occurs in 4.1% of the general population, and chronic tension-type headache and medication overuse headache (MOH) occur in approximately 2.2% and 1.5%, respectively. A proper diagnosis is essential for the treatment of these patients. Treatment should include pathological considerations concerning TTH and MOH, which include peripheral and central mechanisms. Because TTH with MOH carries the worst prognosis, more clinical studies focusing on the complex interaction and treatments of TTH and MOH are needed.

Introduction

Tension-type headache (TTH), especially the chronic form, has a significant comorbidity and an indirect impact, which adds to the burden of disease [1]. Medication overuse headache (MOH) is also a significant public health concern that is characterized by the dependence on acute medications and is refractory to preventive medications [2]. Few studies have been done that describe the association between MOH and TTH. TTH is typically a bilateral headache with a pressing or band-like quality of low to moderate intensity. The major difference between the first International Headache Society's International Classification of Headache Disorders (ICHD) and ICHDII is the subdivision of TTH into infrequent and frequent subtypes [3,4]. The infrequent subtype occurs less than once per month. This subtype is of low impact with minimal health care utilization. In contrast, frequent TTH occurs between once per month to 14 days per month, and chronic tension-type headache (CTTH) occurs 15 days or more a month. High frequency TTH is associated with a high consumption of over-the-counter analgesics and absenteeism compared with healthy controls [5].

There are many reasons why patients who suffer from TTH may overuse medications. Prolonged or frequent TTH may result in medication overuse (MO). Poor stress coping

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mechanisms or pain intolerance may result in a greater tendency to overuse. A high frequency of attacks and a desire to function at work or school are common reasons. Patients with TTH are often not educated about the potential for MO by their physician. Furthermore, patients who suffer from TTH are less likely to seek medical care and may resort to excessive use of over-the-counter analgesics. Patients with comorbid migraine may mistake their TTH for an imminent migraine and treat early as instructed by their physician. Alternatively, behavioral influences such as reinforcement properties of pain relief, psychopathology, and physical dependency are other factors associated with MO [6,7]. This article reviews our current understanding of TTH in the presence of MOH.

Epidemiology

Chronic daily headache (CDH) is defined as a primary headache lasting more than 4 hours on more than 15 days per month. CDH occurs in approximately 4.1% of the US population [8]. CTTH and MOH subdivisions occur in approximately 2.2% and 1.5% of the population, respectively [9–11]. TTH is the most prevalent primary headache disorder, with a 1-year prevalence of 63% in men and 86% in women [12]. The existing data and clinical experience suggest that TTH is a risk for the development of MOH. In a longitudinal population-based study assessing the role of acute medications in the transformation of episodic migraine to transformed migraine, any use of barbiturates and opiates was associated with transformed migraine, and NSAIDs were either protective or inducers depending on the frequency [13•]. Similar studies are needed for TTH.

In an Austrian study, 21% of 80 patients suffering from TTH for an average of 21 years in duration showed signs of MOH, requiring withdrawal therapy [14]. Ultimately, the high consumptions of acute medications appear to be less common in population-based samples of patients with CDH than in patients who present to subspecialty headache centers. In one population-based study, CDH occurred in 89 individuals (4.7%) [9]. Of those patients, only 42 were diagnosed with CTTH and 8 had MO. Forty-five subjects were diagnosed with transformed migraine, and 14 of the subjects had MO. This study suggests that MOH is more common in patients who report a history of migraine than those patients that report TTH alone. This relationship was also seen in a meta-analysis summarizing 29 studies comprising a total of 2612 patients with chronic drug-induced headache [15]. The female-to-male ratio of MOH was 3.5:1. Of these patients, 65% reported migraine as their primary headache disorder, whereas 27% reported TTH and 8% reported mixed or other headaches as their primary headaches. To date, it is still unclear why MOH is more frequent in migraine than TTH.

Further studies are needed to elucidate the relationship between MOH in patients with TTH with and without migraine. MOH may be more common in migraine than TTH, as the abuse of analgesics may be driven by the severity of pain and the disability of the associated symptoms. Another possibility is that MOH and migraine may undergo similar mechanisms of central sensitization, which may differ in some regard to biological mechanisms associated with the development of TTH. A recent study explored the interrelation between CTTH with and without MO and migraine [16]. The authors found that bilateral migraine without aura was significantly more frequent in patients with an age of onset of CTTH prior

to the age of onset of MO compared with those with an age of onset in the reverse order. Of note, the prevalence of migraine without aura was not significantly different in those with or without MO in either gender. This suggests that the presence of migraine may not be a major factor in the decision to overuse in patients with CTTH.

Classification, Diagnostic Challenges, and the Phenotype

Medication overuse headache and chronic daily headache

When patients with CDH present for evaluation, the headache diagnosis is not always easy to determine using the ICHD-II, even with the most detailed headache history. Chronic migraine (CM) features can be lost over time, and patients with CTTH may experience pain severities similar to migraine. MO may be associated with autonomic symptoms, and frequent migraine and TTH can coexist. Perhaps the greatest limitation in review of TTH and MOH is that TTH is not a biological-based diagnosis. In one study, TTH was significantly more frequent in migraineurs than individuals without a history of migraine; therefore, underlying and undiagnosed migraine may be a potential confounder in some of the studies [17]. A strict adherence to the appendix criteria for TTH may be beneficial in future studies [3].

MO is defined as 10 days or more of intake of triptans, ergot alkaloids, mixed analgesics, opioids, or combination analgesics, or 15 days or more of analgesics/NSAIDs consistently for 3 months or more. Although both CM and CTTH may be associated with MO, patients cannot be coded for MOH until symptomatic medication is withdrawn and improvements occur. In the case of CTTH, patients are then coded as probable CTTH, probable MOH, and TTH. Once improvements are made, CTTH is discarded and TTH and MOH are kept. If there is no improvement within 2 months, MOH is discarded and CTTH and TTH are kept. The retrospective nature of the classification is problematic and of limited utility in clinical practice.

The appendix criteria allows for broader definitions [3,18]. According to the criteria, MOH diagnosis should no longer require improvement after discontinuation of MO, but should be given to patients if they have a primary headache plus ongoing MO. According to the criteria, the term *probable MOH* should be discarded. One study compared the diagnosis of a sample of patients with CDH based on the ICHD-II and the new revised criteria [19]. Of the patients, 91% received a combination of diagnoses, and 76% received a probable diagnosis: 47% had probable CM with probable MOH, 28% had probable CTTH with probable MOH, 20% had CTTH, and 3.8% had CM. With the new appendix criteria, 88.5% of the patients required one diagnosis: 66% were classified as MOH, 17% had CTTH, and 6.7% had migraine. However, proponents argue to maintain the 2-month criteria in the ICHD-II, because the clinical situation at 2 months is a predictor of good outcome of 1-year drug withdrawal [20].

According to a study conducted by Katasarva et al. [21], the clinical features of MOH depend on the drug overused and the primary headache type. Ninety-six patients who suffered at least one headache 10 days per month and who took some kind of symptomatic medication 10 days per month underwent withdrawal from their acute medications in a

prospective study. MOH was diagnosed in patients who had significant improvement 1 month after withdrawal therapy. Of the patients, 71% had migraine headache, 14% had TTH, and 15% had both TTH and migraine. The mean duration of the primary headache was 22 years, and the mean duration of drug overuse was 6.5 years. Patients who overused analgesics and ergots were more likely to have a typical daily TTH, and those overusing triptans were more likely to have a migraine-like daily headache. All patients with TTH as their primary headache type developed a CTTH-like daily headache. In addition to the head pain, MO may result in sleep disturbances, restlessness, anxiety, depression, gastrointestinal symptoms, and concentration problems [22].

Ruling out secondary disorders

Several diagnostic challenges occur when patients present with daily tension-like headache [23]. It is first important to distinguish between primary and secondary headache disorders. A headache with tension-like characteristics that occurs for the first time in close temporal relation to another disorder known to cause headache and improves upon resolution of that disorder is consistent with the diagnosis of a secondary headache. One example of secondary headaches, which may be known to mimic TTH and CTTH, is cervicogenic headache; however, it is distinguished by its unilaterality and trigger point. Chronic posttraumatic headaches are often of the tension-type phenotype and are diagnosed historically [24]. Intracranial hypertension typically presents with migraine features but may present with a dull bilateral diffuse headache without migrainous features. Brain tumors are rare causes of daily tension-like headache, but should be considered if of new onset in older patients [25]. Sinus or eye disease, temporomandibular disease, and psychiatric disease are other important causes. To diagnosis sinus disease, purulent discharge and fever should be present. Careful history taking, examination (including a particular sensitivity to red flags), and diagnostic evaluation are required to rule out these disorders, which may be aggravated by MO and may further complicate the diagnosis.

Pathophysiology and Clinical Implications

TTH is an ill-defined heterogeneous syndrome, which is often diagnosed by the absence of migrainous features. The reason for this is that we know very little about the pathophysiology of TTH. It is believed that peripheral myofascial and central mechanisms result in dysregulation of the pain processing pathways [26,27]. In addition, increased muscle tension, which may irritate nociceptors in the cranial and neck muscles, has been suggested as a possible mechanism for TTH [26]. An important consideration in patients is that frequent attacks may progress to CTTH with or without MO. Although often reversible, MOH is a challenge to treat in many patients.

Overview of tension-type headache pathophysiology

Hyperexcitable peripheral nociceptors are a likely etiology of the peripheral mechanism of TTH. Physical triggers may include muscle strain during intense mental activity or poor posture. Infrequent TTH may be the result of peripheral mechanisms, whereas frequent TTH or CTTH may be peripheral and centrally mediated. One study found an increase in central nervous system sensitivity to peripheral nociceptive stimuli such as electrical, thermal, and

pressure stimuli [26]. Qualitatively altered nociception of the stimulus–response function for pain versus palpation pressure in patients with CTTH was also detected. These findings were linked to pericranial tenderness. Because muscle strain is important to maintain CTTH, and CTTH is characterized by hypersensitivity to multiple sensory modalities, both peripheral and central mechanisms are probably involved.

Central sensitization is a process whereby the stimulus required to generate a response decreases, while the amplitude of the response of any given stimulus increases [28]. Repetitive activation of the trigeminal nerve may decrease in nociceptive thresholds and expand the receptive field through functional changes in the neurons of the trigeminal nucleus caudalis. Central sensitization is associated with hyperexcitability in the trigeminal nucleus caudalis. Cutaneous allodynia is the clinical correlate of central sensitization. In a population-based study, the prevalence and severity of cutaneous allodynia were the lowest in severe TTH and other forms of CDH and the highest in transformed migraine [29]. Although central sensitization may be less important for CTTH than CM, evidence suggests that central sensitization may play an important role.

According to several models of CTTH, central sensitization likely occurs at the level of the dorsal horn in the trigeminal nucleus caudalis as a result of prolonged or repeated peripheral nociceptive input from pericranial myofascial tissues [26]. Increased nociceptive input may result in plastic changes in the spinal dorsal horn and peripheral nociceptors [30]. Increased supraspinal pain transmission results in increased pain facilitation and decreased inhibition of pain transmission.

Tension-type headache with medication overuse headache

MO is a modifiable risk factor for CTTH. MOH results in the tendency to treat headaches frequently, which leads to withdrawal headache. In patients with TTH, the most commonly overused medications are simple analgesics, antiinflammatory agents, codeine, combination analgesics, and butalbital-containing analgesics. Acute antimigraine medications such as triptans and dihydroergotamine (DHE) may be overused in patients with comorbid migraine headache. The quantity, duration of use, and type of symptomatic medication are factors associated with the development of MOH. Clinically, excessive use of analgesics may produce a mild euphoria, sedation, and other psychotropic effects that facilitate abuse and addiction.

Surmounting evidence suggests that MOH occurs through multiple mechanisms. Aspirin and paracetamol exert their effects preferentially on peripheral receptors [15]. Repetitive activation of the trigeminal nerve associated with peripheral sensitization may lead to central sensitization. Evidence for central sensitization in MOH includes increasing headache frequency, expansion of headache area, and cutaneous allodynia [31]. MOH may be the result of direct medication effects on central nervous system nociceptive inhibitory pathways. Furthermore, MOH produces changes on a cellular level and within the periaqueductal gray matter and other supraspinal structures [31,32]. One study of patients with CTTH suggests that serotoninergic activity may be associated with MO based on serotonin transporter protein gene–linked polymorphic region genotype analyses [33]. Although family history may be less reliable, one study suggests that a family history of

chronic headache and MO are risk factors for CDH [34]. The genetic and molecular factors of TTH, which protect or predispose patients to MO, deserve further exploration.

Receptor and enzyme physiology contribute to the dysfunction that characterize MOH and may result in tolerance and dependence. Tolerance occurs when a subject's reaction to a drug decreases so that increased doses are required to achieve the same effect. Tolerance may lead to physical dependence, which is associated with withdrawal symptoms upon discontinuation of acute medications.

Routine exposure to a drug induces changes in receptor expression through alterations in DNA transcription [35]. These changes depend on the concentration of the drug, the length of exposure, and the type of receptor. Butalbital is a common drug used to treat TTH and has a high potential for addiction. Butalbital also acts on GABAergic (γ-aminobutyric acid) receptors and induces enzymatic changes. Butalbital produces tolerance and dependence. Pharmacokinetic tolerance develops over days secondary to enzyme induction, whereas pharmacodynamic tolerance develops over weeks to months [36]. Aspirin overuse results in alterations in cyclooxygenase 1 and 2 enzyme induction. Generally, enzymatic changes are slower than receptor changes. This was clinically evident in one study in which the mean duration until the onset of MOH was shortest for triptan overuse (1.7 years) and the longest for analgesic overuse (4.8 years) [37].

Opiates should be avoided in patients with TTH. It is important to recognize that 10% of codeine is metabolized into morphine. In rodent studies, morphine exposure has been associated with increased sensitivity to pain [38]. Peripherally, morphine has been shown to produce increased expression of excitatory neurotransmitters in primary afferent fibers evaluated in the dorsal root ganglion, increased calcitonin gene–related peptide expression, and enhanced release. Centrally, there is an increase in the excitatory neurotransmission at the level of the dorsal horn and the trigeminal nucleus caudalis. Further neuroadaptive processes include enhanced descending pain facilitation as a consequence of prolonged sustained opiate delivery.

MOH has been defined as a biobehavioral disorder by Saper et al. [7]. They hypothesized that the initiation and sustaining dynamics of MOH include psychological and behavioral factors in addition to pain. Several psychological states may contribute to the overuse of acute medications, including fear of headache (cephalgiaphobia), anticipatory anxiety, obsessional drug-taking behaviors, and psychological drug dependence. The willingness and commitment to discontinue overused medications and to maintain appropriate medications depend on motivational factors. Axis II personality disorders, which are sometimes diagnosed in patients with MOH, often have behavioral issues of entitlement, control, and defiance regarding pain. The emotional state of the MOH sufferer may include distress and may contribute to the escalation of pain. Not all patients with MOH exhibit biobehavioral complexities; however, it is important to appropriately identify these patients because of the negative impact on the doctor–patient relationship and dire need for a tailored treatment approach.

It is important to diagnose and evaluate psychiatric comorbidity in patients with CTTH and MOH. Butalbital may be abused because of its anxiolytic properties, masking anxiety disorders [7,36]. A personal history of substance abuse is a risk factor for MOH. Calabresi and Cupini [39] suggested that MOH may have similarities with drug addiction. The comparison is supported by similar pathways, including the ventral tegmental area, biochemical changes induced by reward and memory, and cognitive impulsivity. A positron emission tomography study identified areas of hypometabolism in the pain processing structures of the brain in patients with MOH and a history of episodic migraine [40]. These findings were reversible within 3 weeks after discontinuation of analgesics, except in individuals using combination analgesics and/or ergotamine-caffeine preparations. The authors suggested that persistent orbitofrontal hypometabolism, seen in drug dependence, may be a risk factor for the development of recurrent MOH. Ultimately, the risks associated with MOH likely involve pharmacogenetic, environmental, and social factors. It is important to note that MOH patients differ from individuals addicted to alcohol or other drugs, because patients with MOH develop dependence on acute medications primarily to provide pain relief and improve function.

Clinical Management: Tension-type Headache with Medication Overuse Headache

Treatment approaches can be categorized as pharmacological and nonpharmacological strategies. The goals of treating MOH include prevention, the reduction of headache frequency and MO, and an improvement in the response to acute and preventive treatments. The goal of the medication history is to determine how many days in a typical month the patient takes acute analgesics for any type of headache or other painful disorders. The clinician should obtain the types of acute analgesics, the use of combinations, doses, and frequency. The history should also include identifying periods of medication escalation and identifying the symptomatic medication efficacy on initial use and with current use. The diagnosis and treatment of psychiatric comorbidity and substance abuse disorders are important. In addition to taking a good history, patient education is essential. One study of MOH, with patients of low medical need, found no significant differences between the group that was treated with strong advice and education about the risk of MO versus those treated with an inpatient and outpatient detoxification [41]. Acute symptomatic medications should be limited to 2 days per week. Pain contracts, restricted narcotic and butalbital prescriptions, and permitted communication with other physicians and pharmacists may be effective ways to improve long-term success rates.

The decision to initiate an abrupt versus gradual medication withdrawal strategy should be tailored according the individual patient, the acute medication of abuse, and potential withdrawal symptoms, although many clinicians favor an abrupt withdrawal [42]. Inpatient detoxification programs may be preferred for patients with psychiatric comorbidities. MO of butalbital, sedatives, tranquilizers, or opiates is another indication for inpatient management. Severe withdrawal symptoms and serious medical side effects (eg, gastrointestinal bleeding, seizures) are other clinical indications.

Early preventive treatment is a new concept, which may be more effective in treating total headache suffering compared with abrupt withdrawal [43]. This was evident in a randomized, double-blind, placebo-controlled study of topiramate [44]. In a subgroup analysis, although medication use did not decrease in the topiramate group compared with placebo, topiramate treatment resulted in a reduction in the number of migraine days in the MO population by 3.5 ± 7.1 from baseline in the last 4 weeks of the double-blind phase compared with placebo, with an increase of 0.8 ± 4.8 days ($P = 0.03$). Similar benefits may occur in CTTH with MOH; therefore, a trial of prevention medications should be initiated. The tricyclic antidepressants are the most studied class of agents, and there is evidence for the effectiveness of these agents in reducing headache frequency and severity in the episodic and chronic subtypes [45]. One may also consider occipital nerve blocks as part of an outpatient treatment regimen for low-risk patients.

Standard inpatient protocols are more established for migraine with MO. They include treatments with hydration, NSAIDs, aspirin, repetitive intravenous DHE, neuroleptics, intravenous steroids, intravenous valproic acid, clonidine, benzodiazepines, and conjunctive behavioral treatments [46]. Although a randomized double-blinded clinical trial is lacking, withdrawal symptoms may be treated with intravenous lidocaine infusions in patients with MOH, especially those who have contraindications to intravenous DHE [47•]. Nonpharmacological methods may be of benefit in patients with MOH. Grazzi et al. [48] demonstrated that the addition of behavioral treatment can enhance drug treatment evidenced by symptom reduction and relapse prevention.

Studies with the aim of elucidating long-term relapse rates and potential predictors of relapse following successful withdrawal therapy have been useful in providing prognostic indicators, which may guide the clinical management of patients with MOH. In one study that followed 96 patients with MOH, the relapse rates at 1 and 4 years were 41% and 45%, respectively [49]. The study identified several important risk factors. The relapse rate depended on the type of analgesics being misused: 71% for analgesics, 27% for ergots, and 21% for triptans. The relapse rate also depended on the type of primary headache. The relapse rate was lower for patients with migraine (32%) and higher for patients with a combination of migraine and TTH (70%) and TTH alone (91%). In another prospective study of 38 patients with a 5-year follow-up, the relapse rate was 40%, and TTH was also a predictor of relapse [50]. As a consequence of high relapse rates in patients who suffer from MOH and TTH, close follow-up is suggested within the first year to improve success rates.

Conclusions

TTH is a primary headache disorder with low health care utilization compared with migraine. There is a small yet significant subset of patients with TTH who overuse symptomatic medications. Ultimately, TTH with MOH is a serious health care problem associated with a poor prognosis and high likelihood for relapse. A greater understanding of the biological basis of CTTH is warranted to distinguish it from other headache disorders and to determine the role of MO in the course of the disease.

Psychopathology, dependency, and biological mechanisms translate to clinical challenges in approaching TTH and MOH. Patient education and open communication between the physician and the patient are paramount for effective clinical management. In addition, longitudinal studies and comparative controlled studies that assess the therapeutic efficacy of commonly used treatment strategies are necessary.

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References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

• Of importance

•• Of major importance

1. Lenaerts M. Burden of tension-type headache. Curr Pain Headache Rep. 2006; 10:459–462. [PubMed: 17087872]
2. Silberstein S, Liu D. Drug overuse and rebound headache. Cur Pain Headache Rep. 2002; 6:240–247.
3. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders, 2nd edn. Cephalalgia. 2004; 24(Suppl 1):1–60.
4. Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Cephalalgia. 1988; 8(Suppl 7):1–96.
5. Lyngberg AC, Rasmussen BK, Jorgensen T, Jensen R. Secular changes in health care utilization and work absence for migraine and tension-type headache: a population based study. Eur J Epidemiol. 2005; 20:107–114.
6. Lake A. Medication overuse headache: biobehavioral issues and solutions. Headache. 2006; 46(Suppl 3):S88–S97. [PubMed: 17034403]
7. Saper JR, Hamel RL, Lake AE. Medication overuse headache (MOH) is a biobehavioral disorder. Cephalalgia. 2005; 25:545–546. [PubMed: 15955043]
8. Scher, Al; Stewart, WF.; Ricci, JA.; Lipton, RB. Factors associated with the onset and remission of chronic daily headache in a population-based. Headache. 1998; 38:497–506. [PubMed: 15613165]
9. Castillo J, Munoz P, Guitera V. Epidemiology of chronic daily headache in the general population. Headache. 1999; 39:190–196. [PubMed: 15613213]
10. Schwartz BS, Stewart WF, Simon D, et al. Epidemiology of tension-type headache. JAMA. 1998; 279:381–383. [PubMed: 9459472]
11. Pascual J, Colas R, Castillo J. Epidemiology of chronic daily headache. Curr Pain Headache Rep. 2001; 5:529–536. [PubMed: 11676887]
12. Rassmussen BK, Jensen R, Schroll M, Olesen J. Epidemiology of headache in a general population: a prevalence study. J Clin Epidemiol. 1991; 44:1147–1157. [PubMed: 1941010]
13. Bigal ME, Serrano D, Buse D, et al. Acute migraine medications and evolution from episodic to chronic migraine: a longitudinal population-based study. Headache. 2008; 48:1157–1168. [PubMed: 18808500] Although this study did not follow the evolution from TTH to CTTH, the inducing power of barbiturates and opiates in the transformation of episodic migraine into chronic migraine warrants caution in the treatment of TTH.
14. Schnider P, Aull S, Feucht M, et al. Use and abuse of analgesics in tension-type headaches. Cephalalgia. 1994; 14:162–167. [PubMed: 8062356]

15. Diener, HC.; Dahlof, CGH. Headache associated with chronic use of substances. In: Olesen, J.; Tfelt-Hansen, P.; Welch, KMA., editors. The Headaches. edn 2.. Philadelphia: Lippincott Williams and Wilkins; 1999. p. 871-878.
16. Aaseth K, Grande RB, Lundqvist C, et al. Interrelation of chronic tension-type headache with and without medication overuse and migraine in the general population: the Akershus study of chronic headache. Cephalalgia. 2009; 29:331–337. [PubMed: 19220315]
17. Ulrich V, Russell M, Jensen R, Olesen J. A comparison of tension-type headache in migraineurs and in nonmigraineurs: a population-based study. Pain. 1996; 67:201–206.
18. Headache Classification Committee of the International Headache Society. New appendix criteria open for a broader concept of chronic migraine. Cephalgia. 2006; 26:742–746.
19. Sancisi E, Cevoli S, Pierangeli G, et al. Application of ICHD-II and revised diagnostic criteria to patients with chronic daily headache. Neurol Sci. 2007; 28:2–8. [PubMed: 17385089]
20. Ghiotto N, Sances G, Galli F, et al. Medication overuse headache and applicability of the ICHD-II diagnostic criteria: 1-year follow-up study (CARE I protocol). Cephalalgia. 2009; 29:233–243. [PubMed: 19025549]
21. Katasarva Z, Fritsche G, Muessig M, et al. Clinical features of withdrawal headache following overuse of triptans and other headaches drugs. Neurology. 2001; 57:1694–1698. [PubMed: 11706113]
22. Mathew NT, Kurman R, Perez F. Drug induced refractory- clinical features and management. Headache. 1990; 30:634–638. [PubMed: 2272811]
23. Bigal M, Lipton RB. Tension-type headache: classification and diagnosis. Curr Pain Headache Rep. 2005; 9:423–429. [PubMed: 16282043]
24. Lew HL, Lin PH, Fuh JL, et al. Characteristics and treatment of headache after traumatic brain injury: a focused review. Am J Phys Med Rehabil. 2006; 85:619–627. [PubMed: 16788394]
25. Forsyth PA, Posner JB. Headaches in patients with brain tumors: a study of 111 patients. Neurology. 1993; 43:1678–1683. [PubMed: 8414011]
26. Bendtsen L. Central sensitization in tension-type headachepossible pathophysiological mechanisms. Cephalalgia. 2000; 20:486–508. [PubMed: 11037746]
27. Jensen R. Mechanisms of tension-type headache. Cephalalgia. 2001; 21:786–789. [PubMed: 11595014]
28. Dodick DW, Silberstein SD. Central sensitization theory of migraine: clinical implications. Headache. 2006; 46(Suppl 4):S182–S191. [PubMed: 17078850]
29. Bigal MF, Ashina S, Reed ML, et al. Prevalence and characteristics of allodynia in headache sufferers a population study. Neurology. 2008; 70:1525–1533. [PubMed: 18427069]
30. Ji RR, Woolf C. Neuronal plasticity and signal transduction in nociceptive neurons: implications for the initiation and maintenance of pathological pain. Neurobiol Dis. 2001; 8:1–10. [PubMed: 11162235]
31. Cupini L, Calabresi P. Medication-overuse headache: pathophysiological insights. J Headache Pain. 2005; 6:199–202. [PubMed: 16362663]
32. Ayzenberg I, Obermann M, Nyhuis P, et al. Central sensitization of the trigeminal and somatic nociceptive systems in medication overuse headache mainly involves cerebral supraspinal structures. Cephalalgia. 2006; 26:1106–1114. [PubMed: 16919061]
33. Park JW, Kim JS, Kim YI, et al. Serotoninergic activity contributes to analgesic overuse in patients with chronic tension-type headache. Headache. 2005; 45:1229–1235. [PubMed: 16178954]
34. Cevoli S, Sancisi E, Grimaldi D, et al. Family history of chronic headache and drug overuse as a risk factor for headache chronification. Headache. 2009; 49:412–418. [PubMed: 19267785]
35. Diener, HC.; Limmroth, V.; Katsarava, Z. Medication overuse headache. In: Goadsby, PJ.; Silberstein, SD.; Dodick, DW., editors. Chronic Daily Headache for Clinicians. Hamilton, Ontario, Canada: BC Decker, Inc; 2005. p. 117-127.
36. Young WB, Siow HC. Should butalbital-containing analgesics be banned? Yes. Curr Pain Headache Rep. 2002; 6:151–155. [PubMed: 11872187]
37. Limmroth V, Katasarva Z, Fritsche G, et al. Features of medication overuse headache following overuse of different acute headache drugs. Neurology. 2002; 59:1011–1014. [PubMed: 12370454]

38. Felice M, Porreca F. Opiate-induced persistent pronociceptive trigeminal neural adaptations: potential relevance to opiate-induced medication overuse headache. Cephalalgia. 2009 May 11. (Epub ahead of print).
39. Calabresi P, Cupini L. Medication-overuse headache: similarities with drug addiction. Trends Phamacol Sci. 2005; 26:62–68.
40. Fumal A, Laureys S, Di Clemente L, et al. Orbitofrontal cortex involvement in chronic analgesic-overuse headache evolving from episodic migraine. Brain. 2006; 129:543–550. [PubMed: 16330505]
41. Rossi P, Di Lorenzo C, Faroni J, et al. Advice alone vs structured detoxification programmes for medication overuse headache: a prospective, randomized, open-label trial in transformed migraine patients with low medical needs. Cephalalgia. 2006; 26:1097–1105. [PubMed: 16919060]
42. Reljia G, Granato A, Bratina A, et al. Outcome of medication overuse headache after abrupt in-patient withdrawal. Cephalalgia. 2006; 26:589–595. [PubMed: 16674768]
43. Hagen K, Albretsen C, Vilming ST, Salvesen R, et al. Management of medication overuse headache: 1 year randomized multicentre open-label trial. Cephalalgia. 2008; 29:221–232. [PubMed: 18823363]
44. Diener HC, Bussone G, Van Oene JC, et al. Topiramate reduces headache days in chronic migraine: a randomized, double-blind, placebo-controlled study. Cephalalgia. 2007; 27:814–823. [PubMed: 17441971]
45. Stillman M. Pharmacotherapy of tension-type headaches. Curr Pain Headache Rep. 2002; 6:408–409. [PubMed: 12207854]
46. Dodick DW, Silberstein SD. How clinicians can detect, prevent, and treat medication overuse headache. Cephalalgia. 2008; 28:1209–1217.
47. Marmura M, Rosen N, Abbas M, Silberstein SD. Intravenous lidocaine in the treatment of refractory headache: a retrospective case series. Headache. 2009; 49:286–291. [PubMed: 19222600] This retrospective case series suggests that intravenous lidocaine may be effective for the inpatient management of MOH. This may be of particular importance for patients with MOH and contraindications to intravenous DHE.
48. Grazzi L, Andrasik F, D'Amico D, et al. Behavioral and pharmacological treatment of transformed migraine with analgesic overuse: outcome at 3 years. Headache. 2002; 42:483–490. [PubMed: 12167136]
49. Katasarva Z, Muessig M, Dzagnidze A, et al. Medication overuse headache: rates and predictors for relapse in a 4-year prospective study. Cephalalgia. 2005; 25:12–15. [PubMed: 15606564]
50. Schnider P, Aull S, Baumgartner C, et al. Long term outcome of patients with headache and drug abuse after inpatient withdrawal: five year follow-up. Cephalalgia. 1996; 16:481–485. [PubMed: 8933992]